REMARKS

Status of the Claims

Claims 12-16 and 18-26 are pending in the present application. Claim 12 is independent. Claims 20-22 and 24 stand withdrawn as being drawn to non-elected inventions.

Claims 1-11, 17 and 27 were previously cancelled without prejudice or disclaimer of the subject matter contained therein. Claim 12 has been amended and finds support at least at page 6, lines 11-14 of the Specification as filed. Thus, no new matter has been added by way of amendment to the claims.

Reconsideration of this application, as amended, is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 12-16, 18, 19, 23, 25 and 26 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. This rejection is respectfully traversed.

In order to expedite prosecution of the present application, Applicants have amended claim 12, as suggested by the Examiner at page 3 of the Office Action to recite culturing bone marrow cells or cord blood-derived cells with fat cells, fat precursor cells, and somatic stem cells isolated from mammalian fat tissues (at least supported at page 6, lines 11-14 of the Specification as filed).

Applicants respectfully submit that the claims, as amended, comply with 35 U.S.C. § 112, first paragraph. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 12-16, 18, 19, 23, 25 and 26 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Application Publication No. 2002/0142457 to Umezawa et al. (hereinafter "Umezawa") in view of U.S. Patent No. 4,963,489 to Naughton et al. (hereinafter "Naughton") and further in view of Egger et al., *Nature*, 2004, 429:457-63 (hereinafter "Egger"), Bonnet et al., *Clin. Exp. Med.* (hereinafter "Bonnet"), Gilmore et al., *Exp. Hematol.*, 2000 (hereinafter "Gilmore"), and Lee et al., *Blood*, 2004 (hereinafter "Lee"). This rejection is respectfully traversed.

None of the cited references, either alone or in combination, teach all of the elements of claim 12, as amended. In particular, the combined teachings of the cited references do not teach co-culturing bone marrow cells or cord blood-derived cells with a combination of fat cells, precursor cells, and somatic stem cells.

Naughton, which is relied on for allegedly disclosing stromal cells comprising fat cells, (adipocytes), teaches co-culturing bone marrow cells with isolated fibroblasts "with or without additional cells", as discussed in the March 24, 2010, response. Accordingly, Naughton does not teach or suggest co-culturing bone marrow cells with the described isolated mixture of fat cells, precursor fat cells, and somatic stem cells. Accordingly, the combination of the teachings of the cited references does not render claim 12 obvious, or the dependent claims 13-16 and 18-26, which incorporate all of the elements of independent claim 12, obvious.

The effect of the claimed invention as compared to the teachings of Umezawa is that the claimed invention results in direct differentiation of cells (bone marrow cells or cord blood-derived cells) into myocardial precursor cells and/or myocardial cells. In contrast, Umezawa first treats cells with a DNA-demethylating agent to "reset" the genes on the chromosome and obtain immature cells, that is, cells having the potential to differentiate into cardiomyocytes (Umezawa, page 8, paragraph [0132]; page 19, paragraphs [0321]-[0323]; page 20, paragraphs [0335]-[0341]; page 21, paragraphs [0346]-[0347]; and page 22, paragraph [0360]).

Such a "reset" is not always achieved and the frequency of reset is sometimes low (page 19, paragraph [0321]). Further, Umezawa causes forced expression of transcription factors related to cardiomyogenic differentiation (Umezawa, page 8, paragraph [0132]; and EXAMPLES 6 and 7). These steps are not required for the claimed invention to produce myocardial precursor cells or myocardial cells, and the claimed invention provides a practical technique for easily inducing mammalian bone marrow cells or cord blood-derived cells and fat tissues to differentiate into myocardial cells *in vitro* (the present Specification, page 2, lines 22-29).

In addition, the cardiomyocytes obtained by Umezawa can beat spontaneously about 2 weeks after initiation of the culture (for example, Umezawa, page 19, paragraph [0323]), and after culturing 2-3 weeks, the cardiomyocytes are mainly sinus node cells. After culturing for more than 4 weeks differentiation into ventricular cardiomyocytes is induced (page 8, paragraph

[0134]). A culturing period of more than 4 weeks is too long to be applicable to the purposes of regenerative medicine.

In contrast, the myocardial precursor cells and/or myocardial cells obtained by the claimed methods can beat spontaneously 7 days after initiation of the culture (the present Specification, page 9, lines 19-20). In a later report by a research group including the present inventors (Yamada, Y. et al., Biochemical and Biophysical Research Communications 353: 182-188, 2007, submitted in the IDS filed March 13, 2009 (hereinafter "Yamada")), myocardial cells were obtained according to the claimed methods, specifically by co-culturing brown adipose tissue cells (BATDC) and human umbilical cord blood mononuclear cells (CBMNC) (Yamada, page 183, left column, last 5 lines). The myocardial cells obtained were MLC2V-positive and MLC2A-negative cells (that is, ventricular cardiomyocytes) after co-culturing for 3 days (Yamada, page 185, Fig. 2), and the research group concluded that three days of co-culturing was most effective to produce CM (cardiomyocytes) from e-CBC (educated umbilical cord blood cells) and improve the CM function (page 185, left column, last 3 lines). Such short-term co-culturing to achieve the desired effect is very advantageous in the field of regenerative medicine.

Thus, as the teachings of the cited references, taken alone or together, do not teach all of the claimed elements (*e.g.*, co-culturing bone marrow cells or cord blood-derived cells with a combination of fat cells, precursor cells, and somatic stem cells), Applicants respectfully request that the rejection of claims 12-16, 18, 19, 23, 25 and 26 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Linda T. Parker, Ph.D., Registration No. 46,046 at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

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Respectfully submitted,

By _____

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